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CONGENITAL CHLORIDE DIARRHEA IN A TURKISH BOY*

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Congenital chloride diarrhea (CCD), first described in 1945, is a rare, autosomal-recessively inherited disease. It is characterized by chronic, watery diarrhea with a high fecal chloride concentration, hyponatremia, hypokalemia, and hypochloremic metabolic alkalosis. In this report, a 7.5-year-old boy with CCD diagnosed by high fecal chloride concentration is presented. Until now CCD had not been reported from Turkey, although consanguineous marriages are common. *Key words: congenital chloride diarrhea, stool chloride.*

Congenital chloride diarrhea (CCD) was first described by Gamble et al.[1] and Darrow[2] in 1945, when each reported a child with "congenital alkalosis with diarrhea". CCD is a rare disease with autosomal recessive inheritance[3], and is characterized by life-long secretory diarrhea with a high fecal chloride (Cl^-) concentration, retarded growth and development and biochemical findings of hyponatremia, hypokalemia, and hypochloremic metabolic alkalosis[4]. Watery diarrhea is present from birth but often goes unnoticed because the fluid in the diaper is thought to be urine. Thus, many patients may go unrecognized.

Diarrhea in CCD is a consequence of the selective malabsorption of Cl^-, probably situated at the Cl^-/HCO_3^- exchange transport system in the epithelium of the ileum and colon[5,6]. The effect of this defect is watery diarrhea with a high Cl^- and a low HCO_3^- concentration as well as a low pH.

Since its first description, fewer than 100 patients have been reported[7]. Although patients have been reported from various countries[4,7,8], to the best of our knowledge this is the first case reported from Turkey.

Case Report

The patient was seven years and five months old when the diagnosis of CCD was made. He was referred to us because of chronic watery diarrhea since birth. His weight (18.5 kg) and height (117 cm) were both below the 5th percentile. At that time, the diagnosis was made by estimating stool electrolytes (volume 1500 ml/day; Na^+: 101 mEq/L; K^+: 15.3 mEq/L; and Cl^-: 166 mEq/L).

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Reducing substances were absent from the stool, and no pathogens were isolated on stool culture. The stool pH was 5. The serum aldosterone concentration was at the upper limit of normal (310 pg/ml; normal 40-310 pg/ml), while the renin concentration was six times higher than the upper limit of normal (34.3 ng/ml/hour; normal 1.5-5.7 ng/ml/hour). He had been taking KCl supplements since the age of six months, and salicylate (25 mg/kg per day) since six years of age.

His history revealed that he was born as a dizygotic twin at 35 weeks of gestation by cesarean section. His parents were cousins. Prenatal ultrasonographic examination had revealed distended loops of intestines. His birth weight was 2000 g, appropriate with his gestational age. His abdomen was large and distended. He developed diarrhea during his first day of life, and intravenous electrolyte therapy was initiated. A plain x-ray of the abdomen showed dilated and distended loops of intestines. He had hyperbilirubinemia, and an exchange transfusion was performed. Serum electrolytes on the fourth day of life were Na^+: 128 mEq/L; K^+: 5.4 mEq/L; Cl^-: 96 mEq/L; and CO_2 content 30 mEq/L. Table I demonstrates the biochemical findings during follow-up until this writing. He was discharged after a two-week hospitalization. Diarrhea was thought to be due to gastroenteritis, and distended intestinal loops possibly due to Hirschsprung's disease.

Table I: Electrolyte Concentrations (mEq/L) of Serum, Feces and Urine

	Serum				Feces*			Urine		
Age	Na	K	Cl	CO_2	Na	K	Cl	Na	K	Cl
4 days	128	5.4	96	30	–	–	–	7.6	0.5	–
7 days	131	2.6	102	–	–	–	–	–	–	–
6 mos.	127	2.3	62	42	18	25	112	–	–	5
8.5 mos.	118	3	56	38	–	–	–	–	–	–
3 yrs-4 mos.	126	2	90	–	–	–	–	–	–	–
6 yrs.	138	3.7	99	–	–	–	–	–	–	–
7 yrs-5 mos.	137	3	98	–	101	15.3	166	–	–	very low

* Normal volume and ionic composition of feces in infancy: volume 5-10 ml/kg/day; Na 22 mEq/L; K 54 mEq/L; Cl 21 mEq/L[12].

He was hospitalized two more times during the first three years of life at six and 8.5 months of age because of episodes including dehydration, hypoelectrolytemia including hypochloremia, and metabolic alkalosis. At six months of age, the diagnosis of Bartter syndrome was made because of high aldosterone (1800 pg/ml, normal 20-200 pg/ml) and renin (> 25 ng/ml/hour, normal 0.4-3.2 ng/ml/hour) concentrations. During this admission, stool electrolytes were studied and revealed a high chloride concentration which exceeded the sum of fecal sodium and potassium. Although it was thought that the patient might have

CCD at that time, stool electrolyte concentrations were disregarded because of unreliable laboratory methods. Potassium supplementation was started. The sweat chloride test was done three times and found to be within normal limits. Electrolytes studies were not done between hospitalizations. At the age of six years, salicylate therapy was initiated at a dose of 25 mg/kg per day as a prostaglandin synthetase inhibitor with the diagnosis of Bartter syndrome.

Discussion

CCD is characterized by watery diarrhea of intrauterine onset, and the clinical features of the disease vary with the age of the child[4, 7]. Diarrhea sometimes cannot be noticed during the neonatal period because the stools in diapers may be mistaken for urine. Prenatal diagnosis by ultrasonography is possible[9]. It shows maternal polyhydramnios and distended loops of ileum filled with fluid. Although polyhydramnios was not mentioned, our patient had dilated intestinal loops.

Almost all patients with CCD are born preterm with normal weights and lengths for gestational age. The prematurity is presumably a consequence of polyhydramnios[7]. The abdomen is usually distended. Loops of ileum and colon are dilated with air and fluid. The distended abdomen may lead to a misdiagnosis of Hirschsprung's disease[4]. Our patient was also premature with appropriate weight for gestational age, and Hirschsprung's disease was the initial diagnosis because of the dilated intestinal loops with air. Hyperbilirubinemia has been reported in 68 to 100 percent of patients with CCD[4, 7]. Our patient also had hyperbilirubinemia, and an exchange transfusion was performed. The cause of hyperbilirubinemia is not known, although the dehydration may partly contribute to it.

The correct diagnosis of CCD can be made when fecal chloride is measured and exceeds 100 mEq/L in stools and the sum of the Na^+ and K^+ concentrations[5, 7]. Bartter syndrome and cystic fibrosis were ruled out due to the presence of chronic watery diarrhea and repeated normal sweat chloride concentrations, respectively. The severity of the electrolyte disturbance depends on salt intake and the effectiveness of the activation of the renin-aldosterone system, which invariably occurs, as in our patient[5, 7].

There is no specific treatment for CCD. Acute attacks should be treated with intravenous fluid therapy. Oral NaCl (8-10 mEq/kg per day) and KCl (2-3 mEq/kg per day) should be prescribed as maintenance therapy[4, 7, 10]. Our patient was administered 10 mEq/kg per day of NaCl and 3 mEq/kg per day of KCl. Prostaglandin synthetase inhibitor therapy has been given with the suggestion that prostaglandins may be involved in stimulating the renin-aldosterone system in CCD, but the results have been unsuccessful[7, 11]. Although a decline in the plasma renin and aldosterone concentrations was obtained, the watery diarrhea persisted, similar to our patient.

The estimated incidences of CCD in Kuwait and Finland are 7.6 and 10 per 100.000 live births, respectively[4,7]. We can suppose that the incidence of CCD in Turkey is at least at this level because of the high frequency of consanguineous marriages. In addition to testing reducing substances in stool, stool electrolytes must be studied in every neonate with watery diarrhea to rule out CCD. Special attention should be given to neonates with distended abdomens and dilated intestinal loops. The morbidity and mortality are highest during the neonatal and infancy periods, in which the patient cannot regulate water and salt intake. After the neonatal period, hypokalemia, hypochloremia and metabolic alkalosis are common but not inevitable. The final diagnostic criterion is the high fecal concentration of Cl^-[4]. Adequate growth and development depends on adequate fluid and Cl^- supplementation.

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